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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/010,058	12/07/2001	David Reginald Adams	20791	7827

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PATENT LAW DEPARTMENT
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EXAMINER	
BERNHARDT, EMILY B	

ART UNIT	PAPER NUMBER
1624	9

DATE MAILED: 05/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
10/010,058	ADAMS et al.
Examiner	**Art Unit**
Emily Bernhardt	1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 4/15/03 .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-44 is/are pending in the application.

4a) Of the above, claim(s) 36, 37, 43, and 44 is/are withdrawn from consideration.

5) ☒ Claim(s) 14-32 is/are allowed.

6) ☒ Claim(s) 1-13, 33-35, and 38-42 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 8
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Applicants' election of Group I subject matter and in particular the species of claim 15 with traverse in paper no.7 is acknowledged but is not persuasive for more than one reason. First of all the requirement is indeed a restriction with scope of groups specifically delineated. If an election of species requirement was only intended, **only** a species election would have been required in the previous action. Restriction is proper where there is lack of unity of invention and such is not affected by the manner of claiming- i.e. in separate claims or within a single claim. Note 37 CFR 1.141(a) which states two or more independent, distinct inventions may not be claimed in one application. One application includes the possibility of the separate inventions appearing in one claim or in more than one claim. This is also consistent with PCT Rule 13.3 for PCT cases entering the national stage.
As stated in the previous action the resultant compounds embraced by varying A2 rings constitute structurally dissimilar compounds. Placing all such compounds into the same claims is repugnant to scientific classification as they are not art-recognized equivalents in the pharmaceutical art and are separately classified and require separate online searches given the multitude of compounds expected to be generated for this well known (piperazine) ring. Additionally, different issues of

patentability would be raised at the very least in view of the provisos present in main claim 1 directed to excluding particular substituents on piperazine and/or A2 as phenyl ring, as well as the art provided by applicants in the IDS filed 4/15/03- some of which appears to be pertinent to the elected group. Each can support a patent and are capable of having additional uses as evident by the U.S. patents and foreign patents and journal articles of record.

For the above reasons the restriction is deemed proper and is therefore made FINAL.

Claims 1-13,33-35,38-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1.Recitation of a pharmaceutically acceptable .... ester" is of indeterminate scope. While specification defines some groups for esterification of OH groups (see p.10), there is no guidance as to what other sites can be esterified and with what types of esters? Many different compounds can result from the derivitization to such different types of esters and specification provides no guidelines as to what constitutes any one suitable ester other than for OH groups.

2. Method claim 34 is of indeterminate scope as the claim language may read on disorders not yet known to be associated with serotonin 5 HT2 receptors or in ways not yet understood especially since there are many receptor subtypes currently being evaluated. Furthermore how does one determine who is in need and who is not of such "modulation"? What sort of interaction qualifies as "modulating" ? What distinguishes a mammal, the apparent host, in need of such modulation vs. one who is not in need? 5-HT2 receptors may be involved in all diseases so how can one be sure that any use of claim's 1 scope does not infringe claim 34 ?

Claims 1-10,12-13,33-35,38-42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

1.Specification is not adequately enabled for the scope of piperazines claimed which can have a plethora of functional groups including heteroaryl in various moieties as substituents on A2 as aryl or cycloalkyl as well as any and all ester derivatives thereof. Compounds that have been prepared are mainly mono- or disubstituted with halogens, alkoxy, haloakoxy,haloalkyl,cyano,alkyl,COOMe,

benzyloxy with 3 examples of heteroarylalkoxy where the ring is thienyl,furyl and isoxazolyl. Some are tri-substituted with alkenyloxy and halos. Receptor binding is known to be structure-sensitive as evidenced at the very least by applicants' own statement made in the specification (on p.45) that for exemplary compounds of the invention the range in activity varied as much as 100,000-fold. Note In re Surrey 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. Also see MPEP 2164.03 for enablement requirements in cases directed to structure-sensitive arts such as the pharmaceutical art. Also note the criteria for enablement as set out in In re Wands cited in MPEP 2164.01(a),August 2000 edition. Thus given the breadth of the claims, the level of unpredictability in the art and the lack of direction (i.e. working examples) provided as to what other rings,ring systems as heteroaryl (at various locations) and ester derivatives might work, this rejection is being applied.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4,7,9-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Toldy (Abstract provided by applicants). Toldy describes a piperazine compound (as depicted in the abstract) within the instant scope as a participant in a chemical reaction.

Claims 1-3,6,7,9-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Aicher (Abstract provided by applicants). Aicher also describes a piperazine compound (as depicted in the abstract) embraced by the instant claims as a precursor for making pharmaceutical products.

Claims 1-3,5,7,9,12 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Kawamoto (Chemical Abstract provided).
Kawamoto describes 4-nitrophenylmethoxycarbonyl piperazine compounds as precursors for making antibacterial carbapenems. While 2-methyl derivative has been excluded by one of applicants' proviso, note that the references also describes the 2,6 dimethyl derivative. See compound appended to the abstract which was obtained from a computer-assisted search.

Claims 14-32 are allowed over the art of record as there is nothing teaching or suggesting the type of substituion at A2 ring embraced in these claims from a search in the relevant art area. Papageorgiu while disclosing a process of deprotection is drawn to the preparation of compounds excluded by instant provisos.

Applicants mention an earlier IDS has been filed. No evidence of entry of such is seen in the record and there is no IDS statement much less references.

Any inquiry concerning this communication should be directed to Emily Bernhardt at telephone number (703) 308-4714.

A facsimile center has been established for Group 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machine are (703) 308-4556 or (703) 305-3592.

E Bernhardt

EMILY BERNHARDT

PRIMARY EXAMINER

GROUP 1600